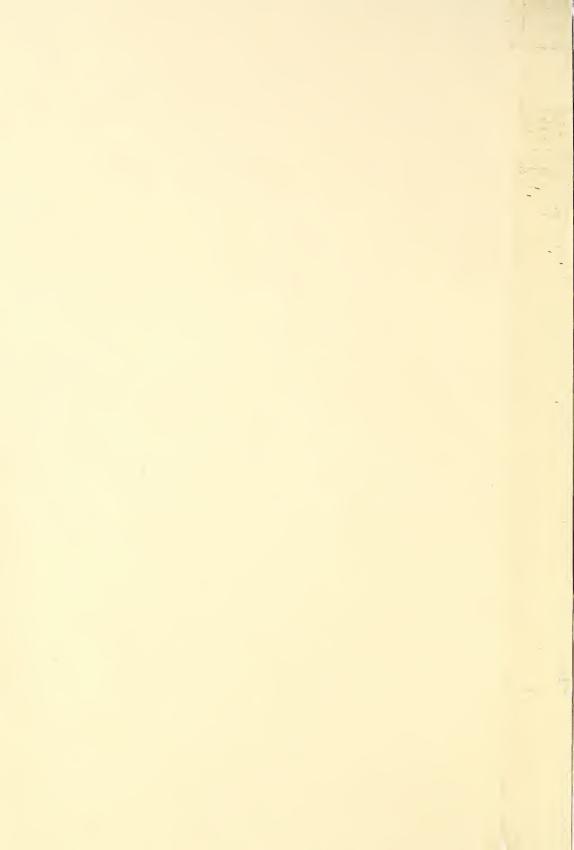
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W. O. ATWATER MEMORIAL LECTURE

1980



Overweight, Obesity, Coronary Heart Disease and Mortality

> Ancel Keys, Ph.D. Professor Emeritus School of Public Health University of Minnesota Minneapolis



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Wilbur Atwater should be remembered for two reasons. He directed the Connecticut Agriculture Experiment Station, the first in the nation, and later founded the Office of Experiment Stations of the U.S. Department of Agriculture. The immense benefits to agriculture and the American economy alone would merit a memorial to Wilbur Atwater. Atwater also brought the training of a chemist to the examination of the human energy metabolism of nutrients and so is often considered to be the person who established the science of nutrition in the United States. This second contribution especially interests me.

Atwater, with the collaboration of Rose and Benedict, developed and applied a human

calorimeter that allowed measurement of the energetics of combustion in the intact human body. He had studied with Voit and Pettenkofer in Munich and returned to America to continue in the German tradition of Liebig, Rubner and the Munich school. Atwater's calorimeter, a direct descendent of Pettenkofer's, opened up new vistas in the United States, inspiring Graham Lusk and Eugene Dubois, among others.

Though Atwater was active in experimentation with the calorimeter, he was even busier with the chemical analysis of foodstuffs and the elaboration of recommendations about the diet. He joined with other leaders of the time in advocating a high protein diet. Table I summarizes some of the more important recommendations for proteins in the diet. The German leaders held that what healthy Germans were eating must be good and necessary. Since careful dietary surveys, first developed in that period, indicated that healthy German men not doing heavy work had average daily protein intakes of 118g1 or 127 g,2 the conclusion was that such protein intakes are necessary. Atwater brought back from Germany Voit's survey method and applied it to American men to conclude that 125 g of protein in the daily diet — more than 20 percent of total calories were needed.3 The theory of the time was that the need for protein increases with the energy expenditure, so Atwater and the German authorities insisted that for men doing heavy work

The twelfth annual W.O. Atwater Memorial Lecture, sponsored by the Agricultural Research Service, U.S. Department of Agriculture, was given August 11, 1980, at the Western Hemisphere Nutrition Congress VI, Los Angeles, California. These lectures commemorate the life and work of Dr. Atwater, who established the science of modern human nutrition in the United States. Through the lectureship, ARS gives special recognition to individuals who have made outstanding contributions to fields of science broadly related to human nutrition, or advanced public understanding of the role of science in meeting world food needs. Reprints may be obtained from The Nutrition Foundation, 888 17th St., NW, Washington, DC 20006.

about 150 g in the daily diet were needed. Table I shows the ideas of Atwater's time and the contrast with the latest recommendations of the Food and Nutrition Board.⁴

Before we smile at the ideas at the turn of the century, let us reflect that for most of history the dietary problem has been to get enough to eat, especially enough protein. The pioneers of the newly developing science of nutrition wanted to set the highest of standards. They insisted on enough food, particularly food rich in the proteins that had just been recognized as indispensable tissue-building nutrients. People did not worry about dietary excesses in those days.

Actuarial Studies of Mortality

It so happened that Atwater's most productive years coincided with the time when the actuaries

companies began to charge extra premiums for gross "overweight," the extra charge commonly being applied to men who were 25 to 30 percent above the average weight of American men of their age and height who had applied for life insurance.

As the years passed, the death claim experience justified the extra premiums demanded by the actuaries. Persons who paid extra premiums because of overweight proved to have unduly high death rates. As has been pointed out repeatedly, however, the life insurance data are seriously flawed. ⁶⁻⁹ In general, only 2 or 3 percent of life insurance applicants have been required to pay extra premiums because of overweight, but all independent surveys show that the actual frequency of the corresponding degree of overweight persons in the population is

TABLE I

Daily Dietary Intake of Protein Recommended for Adult Men Not Engaged in Heavy Work

Authority	Protein (grams)
Voit (1881)	118
Rubner (1902)	127
Atwater (1902)	125
Food and Nutrition Board, NRC/NAS (1959)	70
Food and Nutrition Board, NRC/NAS (1980)	56

of American life insurance companies insisted that thin persons should pay higher premiums for life insurance. Tuberculosis was a major cause of death and the association between low relative weight and the threat of tuberculosis was well-recognized. So the actuaries supported the nutritionists who were urging generosity in food consumption with protein being the all-important nutrient.

In the early 1900's, however, the actuaries began to find that their death claims were indicating excess mortality among their heaviest policy holders. In 1912, the Association of Life Insurance Medical Directors and the Actuarial Society of America published their "Medico-Actuarial Investigation," the analysis of death claims which showed that men in the top of the distribution of weight for given height and age had an excessive death rate. 5 So life insurance

about 6 or 7 percent. Obviously, the overweight persons who apply for life insurance are a self-selected sample. Why do only a minor percentage of persons so overweight as to be subject to extra premiums apply for insurance? It is well-known in the insurance industry that the insured tend to "select against the insurer". This means that many insurance applicants, both thin and fat, do not disclose extra risks they may know or suspect. It is highly probable then, that some persons "rated" because of overweight are bad risks in other respects unknown to the insurance company.

There is an interesting parallel in the history of life insurance for women. In the later part of the last century, very few women applied for life insurance and when they were issued policies they had to pay a higher premium than men. The actuaries said this was justified by the mortality

experience. Around the turn of the century, however, some companies began to offer family policies covering both husband and wife. The number of women who then were covered with life insurance increased dramatically since no extra premium was involved simply for being a woman. The mortality experience subsequently proved that, as we all know now, women in general have a greater life expectancy than men. Obviously, the women who had been applying for policies during the time when they had to pay extra for being a woman were not a proper sample of women in terms of life expectancy.

Another major objection about the data of the life insurance companies is the fact that many of the heights and weights recorded on the applications do not represent actual measurements. When the Society of Actuaries re-examined their data in 1959,10 they were pleased to conclude that as many as 80 percent of the weights recorded were actual measurements - with the applicants "as customarily dressed," including shoes. Further there is no information about the frequency of cases in which weights or state of health were falsified. Economic persuasion being what it is, falsification does occur. The difference between an ordinary life insurance premium and one rated because of overweight or indication of disease is substantial. The insurance agent is paid according to his success in selling policies that are accepted by the underwriter. Examining physicians whose reports may result in policies declined by the company or the applicants are shunned by the agent.

Fortunately, much better data on the relationship of relative weight to mortality are now increasingly available from prospective scientific studies, and shortly I shall show what they tell us, but first we must complete consideration of the insurance industry story.

Determination of Desirable Weight

The Metropolitan Life Insurance Company, with the leadership of its chief actuary, the late Louis Dublin, has been a major source of propaganda about the evils of overweight. That was the source of the tables of so-called "ideal weight," later less presumptuously called "desirable weight". These tables were based on the notion that after growth in height and ossification is completed in the early twenties, there is no

physiological reason for further increase in body weight.¹¹ The fact is, however, that in all but a few primitive peoples the average body weight continues to increase into middle age, so the great majority of people aged 40 would be labeled grossly overweight by that standard. Table II shows the actual weight for given height recommended as "desirable" by the Metropolitan Life Insurance Company.

Dublin considered that the "ideal" weight should be the average weight for given height and sex of applicants for insurance policies issued in their mid-twenties. When he examined the data on the weights of his policy holders in their mid-twenties, however, he found a great range for persons of the same sex and height. He thought, in part at least, that wide distribution reflected differences in body shape or "frame," as he called it. There are no data or body shape or frame type—and this lack continues today but Dublin created three frame "types" very simply. At given height, he divided the distribution of body weights into thirds and labeled these "small," "medium" and "large" frames, alternatively called light, medium and heavy frames. The average weights of those thirds of the distribution were then termed ideal weights for those frame types.

The fact is that the tables of "ideal" or "desirable" weight are arm-chair concoctions starting with questionable assumptions and ending with three sets of standards for "body frames" which were never measured or even properly defined. Unfortunately, those tables have been reprinted by the thousands and are widely accepted as the gospel truth.

In contrast with these Metropolitan Life tables, what are the actual average weights for given heights? Table II summarizes comparisons. From insurance company data it appears that the average American man aged 40 to 49 years applying for insurance is 12 percent over the weight listed as "desirable". More reliable measurements in scientific surveys of American men of that age, such as in the Pooling Project of prospective studies concerned with coronary heart disease, 12 show the average weight for American men aged 40 to 59 years is 17 percent above the desirable weight figure for men of "medium frame". A large study on American railroad men agrees. 13 Our Minnesota

businessmen averaged 14 percent over the "desirable" weight. These facts are popularly interpreted as serious threats to health, a major reason for the "coronary epidemic".

Surveys of Weight and Coronary Disease

Dublin's successor as chief actuary of the Met-

the question as to how representative of the population are the persons who answer such questionnaires and the reliability of their answers. Equally important is the lack of critical multivariate analysis of inter-relationships among variables of interest regarding mortality — blood pressure, cholesterol and other lipids in

TABLE II

Average Weight Percent of American Men Aged 40 to 59 Years: Metropolitan Life Insurance Company "Desirable" Weight for Given Height

Material	Source	Percentage
Life insurance applicants in the U.S.	Society of Actuaries 1959	115.2
Five studies on urban residents in four cities	Pooling Project Group Final Report, 1978	116.7
U.S. railroad employees	Seven Countries Study 1980	115.8
Twin cities men of 1948 followed through 1978	A. Keys and colleagues	113.6

ropolitan Life Insurance Company is first author of a recent paper on findings from 750,000 answers to an American Cancer Society questionnaire.15 The conclusion is that they confirm the view that the risk of early death in general, and from coronary heart disease in particular, is directly related to the relative body weight. This is another example of the fallacy that large numbers can convert bad into good data. Even if the questionnaire data are accepted, the top claim is that persons 30 or more percent above average relative weight have a coronary death rate 55 percent above the average. Only 1.6 percent of the persons in the study, however, were so grossly overweight. This is a long way from the claim that a few extra pounds are a mortal danger.

The Cancer Society questionnaire, distributed by local non-professional volunteers, asked the age, sex, height, weight and smoking habits. During six years, Cancer Society volunteers tried to find out who had died and what was reported as the cause of death. No measurements or medical examinations were involved. Apart from the question of the accuracy of the answers to the question, "How tall are you and what do you weigh?" that approach glosses over

the plasma, occupation, dietary habits, besides relative weight and smoking.

A striking feature of the insurance propaganda is the total absence of any mention of opposing evidence. As soon as it became apparent that the great modern epidemic of our society is coronary heart disease, the word went out that this was caused by overweight. No attention was paid to critical data from non-insurance sources.

In 1948, Yater and colleagues¹⁶⁻¹⁸ published their findings on 866 coronary deaths (450 with detailed autopsies) of U.S. soldiers less than 40 years of age. The relative weights were no different from those of soldiers of the same age killed in military accidents nor were the coronary victims heavier than their fellows when they entered the Army. In 1949, Billings and colleagues¹⁹ reported on patients admitted to hospital with acute myocardial infarction. There was no excess of obese patients. Moreover, the prognosis of the fatter patients proved to be better than that of the others. The most significant facts are those coming from scientific prospective studies on population samples.

Prospective Studies

Prospective studies to find characteristics of people predisposed to coronary heart disease

TABLE III Fate of 284 Minnesota Men, 45 to 55 Years of Age at Entry. after 30 Years When Compared to Mean Body Mass Index.

Status	Number	Mean BMI*	SE
Alive	143	24.76	2.8
Dead	141	25.13	3.2
Coronary Dead	62	25.43	5.0

began in 1947 in Minnesota with middle-aged business and professional men who were to be followed with annual re-examinations.20,21 Similar studies began elsewhere soon after and now we have follow-up data on many thousands of men who were not involved in any commercial relationship and who were given far better and more complete medical examinations than in the insurance business.

Table III summarizes the experience of the Minnesota men with regard to relative body weight at entry and subsequent mortality. In Minnesota in 1947, we were short of money and of understanding of statistical requirements. The number of subjects was so small we had to follow them a long time to get significant numbers of deaths for analysis. As of the end of 1978, we can compare the characteristics of 143 men who died with those of 141 survivors.

It is now commonly agreed that the best measure of relative body weight is the body mass index, the weight divided by the square of the height.²² The average body mass index at entry of the men who died was 1.5 percent greater than that of the survivors through 1978, but that difference is far from being statistically significant. The mean body mass index of the 62 men who died from coronary heart disease was 2.6 percent more than that of the survivors, but that difference could be expected to occur by chance in more than one of five trials.

It can be argued that 143 deaths are not many and if we had found the same mean differences with a sample ten times greater, the difference would have been highly significant. Even the most trifling difference will be statistically significant if the numbers are large enough. In the present case, the finding is that at equal height, the average weight of the men who died from all

causes was 2.6 pounds (1.16 kg) more than the survivors. The average weight of those who died from coronary heart disease was 5 pounds (2.25 kg) more than the survivors. Should we propose that a difference of 5 pounds (2.25 kg) means the difference between survival and death from coronary heart disease?

Now consider some 18-year findings in the Framingham Study in Table IV. The results come from solutions of the multiple logistic equation which finds the coefficients in an exponential equation that best discriminate cases from non-cases. When the entry characteristics and the outcome, case or non-case, are fed into the computer programmed for the equation, not only are the coefficients found, but also their standard errors. The coefficient divided by its standard error is the familiar t-value and the probability that the coefficient is not zero is readily found by consulting a table of t-values.

At Framingham, the development of coronary heart disease, accepting any diagnosis, was positively related to relative body weight, but neither myocardial infarction nor death from that disease was significantly related to relative weight.23 In both sexes, death from all causes was negatively related to relative weight and the relationship was highly significant in men. This means that the threat of death in the follow-up period decreased with increasing relative weight, but we know nothing about the health status of those persons at the preceding examination.

In these prospective studies, the focus is on coronary heart disease and scant attention is paid to mortality in general. Table V summarizes seven reports on major prospective studies in North America. The Pooling Project found an increased risk of coronary disease with over-

TABLE IV

Is Death Related to Body Weight?

The Framingham Study

Death Cause	1	Men		omen	
	Α	В	Α	В	
Coronary	n.s.	n.s.	n.s.	n.s.	
Any	neg.	neg.	n.s.	neg.	
Framingham experience n.s. = not significant,	ce, 18 years, ag neg. = significa	es 45 to 74 who ant in inverse d	en studied. irection		
(A: disregard age, B. smoking, cholesterol, e		holesterol, etc;	B: allow for	age, B.P.,	

weight in younger, but not older men. Perhaps the younger overweight airplane pilots were unduly prone to coronary disease. Conclusions are unwarranted because there was no information on cholesterol or smoking habits. In all the other samples noted in Table V, the incidence of coronary heart disease was not significantly related to relative body weight.

relative body weight is an important coronary risk factor. ^{36,38} Let us return to the most important of all end points — death.

Mathematical Analysis of Mortality Data

Until lately, the common concept promoted by the Metropolitan Life Insurance Company has been that the likelihood of early death is directly

TABLE V
Is Coronary Heart Disease Associated with Overweight?
Answers from Some Major American Prospective Studies

Date	Study	Answer
1963	San Francisco longshoremen ²⁴	no
1963	Western Electric Company employees ²⁵	no
1964	Los Angeles civil servants ²⁶ ten-year follow up	no
1971	Los Angeles civil servants ²⁷ 15-year follow up	?
1975	Western Collaborative Study ²⁸	no
1977	Canadian airline pilots ²⁹ men less than 40 years of age men 40 years of age and older	? no
1978	Pool Five of the Pooling Project ¹² men less than 50 years of age men 50 years of age and older	yes no

Table VI shows the results from six major studies of the same kind in Europe. Not one shows a significant relationship between coronary heart disease and relative body weight. Critical reviews fail to find good evidence that

related to relative body weight. A critical analysis of the 14-year experience of the men in the Chicago Peoples Gas Company Study,³⁹ showed first, mortality was not a positive linear function of relative weight. If anything, the re-

lationship is inverse. Second, more sophisticated analysis indicated a curvilinear relationship with mortality increasing at both extremes of the distribution as indicated in Figure 1.

line, meaning the probability of death decreases with increasing relative weight. On the other hand, when the equation is solved with body mass index as a quadratic, the answer is a

TABLE VI

Is Coronary Heart Disease As	sociated with Overweight?
Answers from Major Prospe	ective Studies in Europe

Date	Study	Answer	
1972	Public utility employees in Norway ³⁰	no	
1975	Men in Stockholm, Sweden ³¹	no	
1975	Men in Gothenburg, Sweden ³²	no	
1976	Men in selected areas of Yugoslavia 33	no	
1977	Senior public servants in England ³⁴	no	
1978	Helsinki policemen ³⁵	no	

The relations shown in this figure are from multiple logistic solutions for the best discrimination between the men who died and those who did not, plotting the probability of death on the ordinate and the body mass index on the abscissa, for men starting at age 45 and for men starting at age 55, holding blood pressure constant. At the top of the figure, a broken straight line and a curved solid line summarize the analysis for men age 55 followed for 14 years. The solid line shows that if the equation is solved to get the best linear fit between relative weight and mortality, the result is a downward slanting

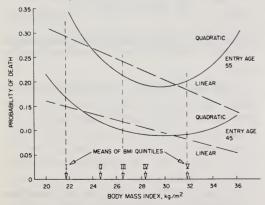


Figure 1: Chicago Gas Company men, 14-year follow-up. Probability of death (all causes) calculated from multiple logistic solutions with the independent variables age, systolic blood pressure and body mass index (BMI) for the linear model and the same variables plus the square of BMI in the quadratic model.¹⁴

curved line which fits the data better. This means that the probability of death is least in the middle of the distribution and rises progressively as the relative weight increases towards either extreme of under- or overweight.

A broken vertical line shows the median body mass index of these Chicago men and it is clear, then, that the lowest mortality is in the region above the average body mass index. The relation for men starting at age 45 is shown in the lower pair of lines. Again, the finding is that if a linear relationship is sought, the probability of death steadily decreases with increasing relative weight. Mathematically, however, the data are best fitted with the curved line and again the indication is that the best prognosis is for men somewhat above the average relative weight.

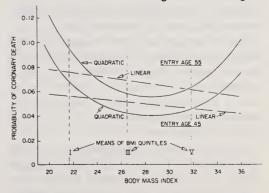


Figure 2: Chicago Gas Company men, 14-year follow-up. Probability of death from coronary heart disease calculated as in Figure 1.¹⁴

This figure concerns all causes of death. Figure 2 shows the Chicago data analyzed in the same way with death from coronary heart disease as the end point. The linear solutions show a non-significant slope downwards, meaning that death from coronary heart disease decreases with relative weight. The mathematical analysis, however, indicates a better fit with the quadratic and, again, the least chance of coronary death at relative weight somewhat above the median and the worst prospect for the most underweight and the most overweight men.

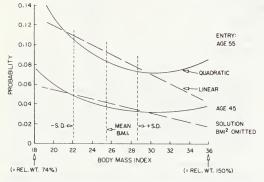


Figure 3: U.S. railroad men, ten-year follow-up. Probability of death (all causes) calculated as in Figure 1.

The Seven Countries findings agree with those on the Chicago men. Figure 3 summarizes the analysis for the U.S. railroad men aged 45 to 55 years at the start of the ten-year follow-up. The linear answer shows decreasing chance of death with increasing relative weight. The more elaborate quadratic solution indicates that it is bad to be overweight, worse to be underweight and best to be somewhat over the average relative weight for men of the same age.

Figure 4 is the counterpart analysis of the 285 deaths in the northern European cohorts of the Seven Countries Study. The downward slope of the linear solutions is less steep and the curvature of the quadratics is less marked, but the general picture is the same as in Chicago and in the U.S. railroad men.

Figure 5 is the corresponding picture for the men in southern Europe in the Seven Countries Study. There were 774 deaths among 5,936 men. The general picture is the same and the conclusion is, again, that the best prospect for avoiding early death is to be somewhat above the average in relative weight.

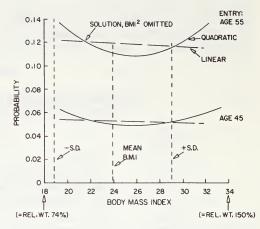


Figure 4: Men in northern Europe, ten-year follow-up. Probability of death (all causes) calculated as in Figure 1.¹⁴

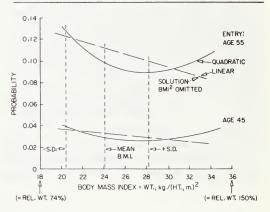


Figure 5: Men in southern Europe, ten-year follow-up. Probability of death (all causes) calculated as in Figure 1.

I trust that soon this more sophisticated approach will be applied to other sets of data from prospective studies. All of the available data show a consistent picture, but it must be emphasized that we have no data on women or on men younger than 40 years at the start of follow-up. This limitation cannot be quickly corrected because the major follow-up studies have concentrated on middle-aged men. The numbers of women and younger men enrolled in these studies are too small for definitive analysis as yet.

Obesity Versus Body Weight

The title of this Atwater Lecture includes the

word "obesity". From what I have presented so far, it may seem that I am equating relative weight with body fatness. Table VII indicates one of the reasons why it is incorrect to assume that

gaining fat, but do not make the mistake of gauging obesity by relative weight. Football players are generally greatly overweight but are not fat. Office workers may be over-fat, that is to

TABLE VII

Correlation (r) between Body Mass Index and
Other Characteristics, White Men Aged 40 to 59 Years¹³

Area	Number	Characteristics				
		Skinfolds	Systolic B.P.	Cholesterol	Smoking	
Finland	1,677	0.79	0.16	0.12	-0.24	
Greece	1,215	0.82	0.28	0.28	-0.22	
Italy	2,480	0.78	0.24	0.21	-0.24	
Netherlands	878	0.70	0.32	0.21	-0.09	
U.S. Railroad	2,571	0.75	0.23	0.09	-0.10	
Yugoslavia	2,932	0.82	0.26	0.22	-0.25	

relative body weight is a reliable measure of fatness or obesity.

Observe the figures in the column headed "skinfolds". About half of the total fat in the body is subcutaneous and this is being measured when skinfold calipers are applied to selected sites on the body. The table shows a highly significant correlation between relative body mass index and the mean skinfold thickness. The average coefficient of correlation is r=0.78, but this means that more than a third of the variance in one variable is not accounted for by the other.

The density of the body is a better measure of the proportion of the body weight accounted for by fat, but the measurement is much too difficult for all but very special studies. In our study on Minnesota men, however, the body density was measured on several occasions. The correlation between body density and relative body weight was r=-0.67, highly significant, but relative weight accounted for only 45 percent of the variance of this best measure of body fatness.

All of this means that body mass index and all other measures of relative weight give very poor estimates of obesity or body fatness, useful only at the far extremes of the distribution. Watch changes in body weight as indicators of losing or

say obese, though not overweight.

Unfortunately, estimates of obesity or body fatness have not been included in prospective studies except those directed from the University of Minnesota. Our Minnesota findings indicate that body fatness is more of a risk factor than is relative body weight, but even so obesity is still only of minor concern in regard to longevity except at the extreme end of the distribution of fatness. In any case, it is essential to take account of other characteristics in evaluating obesity or relative weight as risk factors.

Table VII shows the coefficients of correlation between body mass index and other variables relevant to future health. The correlation is small, but significant with blood pressure, serum cholesterol and cigarette smoking, this last being a negative relation. These correlations must be taken into account in evaluating the independent significance of relative weight.

We and other investigators find that in the absence of hypertension, overweight is not a risk factor at all. Nonetheless, there is a tendency for persons with high blood pressure to be overweight. Such persons should be advised to reduce their weights since blood pressure often drops when weight is lost by the overweight person.

Most of what I have said in this lecture refers to men 40 or more years old. Unfortunately, in the concentration on such persons, the data from good prospective studies on women and on younger men are as yet very scanty. Happily, women and young men have few heart attacks and low death rates. Unhappily, for investigators like myself, this means that very large, long-term studies are needed and we have neither the money nor the personal expectation of longevity to fill this large gap in our personal knowledge.

A few weeks ago, results were published from a ten-year follow-up on middle-aged Swedish women making a substantial increase in our knowledge about obesity and relative weight as risk factors for women. 40 The finding was that for developing coronary heart disease, "only marked obesity constitutes an increased risk". The death rate was not related to relative body weight, but tended to be negatively related to body fatness. This means that the thinner women tended to have a higher death rate.

Conclusions

The conclusions from all the evidence seem obvious. They may be stated in a few words. The idea has been greatly oversold that the risk of dying prematurely or of having a heart attack is directly related to the relative body weight. For middle-aged men, the best prospect for avoiding death in ten or 15 years is to be about average, or a bit over, in relative weight. The risk rises somewhat with departure in either direction from the happy middle ground, but risk increases substantially only at the extremes of under- and overweight.

Data are very scanty on younger men and on women. For middle-aged women, it appears that they are like the men in regard to the risk associated with relative weight. Both extreme under- and overweight seem likely to entail risk, but there is no acceptable evidence that relative body weight has any relevance to future health for women in the middle 80 percent of the relative weight distribution.

None of what I have said means that I favor obesity, especially in our current society which considers fatness to be a cosmetic defect. I am simply talking about physical health. Finally, it must be emphasized that body weight is a poor measure of fatness. \square

Postscript

After this lecture was completed, I saw the latest report from the Framingham Group (P. Sorlie, T. Gordon and W.B. Kannel: Body Build and Mortality: The Framingham Study. *J. Am. Med. Assoc.* 243: 1828-1831, 1980). Their conclusion states." The unselected sample of the Framingham Study shows minimum mortality around the average weight with increased mortality for persons weighing more or less than the average."

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